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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,842	12/07/2001	Jian Ni	1488.131000A	4105

28730 7590 08/06/2004

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EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,842	NI ET AL.	
	Examiner	Art Unit	
	Claire M Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-133 and 152-203* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *62-72,117-126,160-178 and 198-203* is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *36,45,54,75,83,92,100 and 109* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/8/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims rejected are 35,37-44,46-53,55-61,73,74,76-82,84-91,93-99,101-107,110-116,127-133,152-159 and 179-197.

DETAILED ACTION

Response to Amendment

The rejection of claims under 35 USC 112, first paragraph, is moot in view of the cancellation of the claims. Note that new rejections appear below.

The rejection of claims under 35 USC 102(e) and 103 as anticipated by or obvious over US Patent 6,072,047 is withdrawn in view of Applicants' arguments that the patent does not receive priority to parent application 08/815,255, filed 3/12/97. This and the earlier priority application have an insufficient disclosure of the DR5 encoding nucleic acid or protein such that the patent could receive benefit of priority for the instantly claimed subject matter.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 130 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear to what the "heterologous polypeptide" is referring. It is unclear if it refers to an additional polypeptide, in which case wording for the claim such as "...127, which further comprises a heterologous polypeptide" would obviate the rejection. Alternative, it is unclear if it refers to a portion of the claimed polypeptide which is heterologous to the polypeptide of SEQ ID NO:2, in which case identification of to what the polypeptide is heterologous would obviate this rejection.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35, 37-44, 46-53, 55-61, 99, 101-108, 110-116, 152-159 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising an amino acid sequence at least 90% identical to amino acids 1-360 of SEQ ID NO:2, wherein said polypeptide induces apoptosis or binds TRAIL, does not reasonably provide enablement for an isolated polypeptide comprising an amino acid sequence at least 90% identical to amino acids 1-360 of SEQ ID NO:2, wherein said polypeptide binds an antibody with specificity for the polypeptide of amino acids 1-360 of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The amendment to the claims has necessitated this rejection. While being enabled for a polypeptide with a sequence at least 90% identical to SEQ ID NO:2 which induces apoptosis or binds TRAIL, the specification is not enabling for those polypeptides which are bound by an antibody with specificity for SEQ ID NO:2 but do not induce apoptosis or bind TRAIL. There are a very large number of polypeptides which meet the structural requirements of the claim but share no function with SEQ ID NO:2. The specification has not taught how to use such polypeptides. The sharing of an antibody binding site does not confer enablement to a polypeptide. While the skilled artisan could use an antibody that binds SEQ ID NO:2, it would require undue experimentation to us a polypeptide bound by the antibody if that polypeptide did not share the property of inducing apoptosis or binding to TRAIL as disclosed for SEQ ID NO:2.

Claims 73, 74, 76-82, 84-91 and 93-98 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide consisting of the designated amino acid fragment, does not reasonably provide enablement for a polypeptide comprising the fragment where the fragment is not identical to a fragment of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to a polypeptide comprising a sequence at least 90% identical to a fragment, wherein the sequence has a function; however, the claimed polypeptide does not need to have a function. The functional limitation recited in the claims limits the sequence at least 90% identical to a designated fragment of SEQ ID NO:2 instead of limiting the claimed polypeptide. The fragment of claim 73 is the transmembrane domain (TMD), claim 83 is the intracellular domain (ICD), and claim 92 is the death domain (DD). For claims in which the domain is not identical to the disclosed domain sequence of DR5, it is unpredictable how this domain would function out of context even if it were able to function within a "DR5 variant" recited in the claims. While several DD-containing proteins were known in the prior art, mix-and-match domains for the proteins are not shown, and which amino acids can be changed so that the domain will impart a function within a heterologous sequence is not disclosed. The specification provides no working examples of polypeptides comprising only one of the domains recited in the claims. How and if a domain would function within a polypeptide would be dependent on the sequence of the polypeptide and positioning of the domain sequence within the polypeptide. The specification does not provide guidance for the skilled artisan to be able to use a commensurate number of polypeptides as recited without undue experimentation commensurate with the scope of the claims.

Claims 127-133 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide consisting of at least 50 contiguous amino acids of the designated region of SEQ ID NO:2, does not reasonably provide

enablement for a polypeptide comprising the at least 50 contiguous amino acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a polypeptide, but the functional limitation recited in the claims limits the 50 amino acid fragment comprised by the polypeptide instead of the claimed polypeptide itself. The specification does not provide guidance or working examples to allow the skilled artisan to use a polypeptide comprising the fragment even if the polypeptide comprises a binding site for an antibody that binds SEQ ID NO:2. Binding of a polypeptide by an antibody does not alone provide enablement. It would require undue experimentation to use the claimed polypeptide.

Claims 35, 37-44, 46-53, 55-61, 99, 101-108, 110-116, 152-159 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides comprising an amino acid sequence having at least 90% or 95% sequence identity with a particular disclosed sequence, which polypeptide binds an antibody with specificity for the polypeptide of amino acids 1-360 of SEQ ID NO:2. The claims are to a genus of polypeptides, only a small number of which have been described. For example, the portion of the polypeptide comprising the region with the specified identity to SEQ ID NO:2 is not necessarily the portion which is bound by the antibody. Such polypeptide have not been described. Further, because the claims use the open language of a "polypeptide comprising", the claims are structurally very broad and include polypeptides in which the recited activity is not due to the amino acid sequence at least 90% identical to amino acids 1-360 of SEQ ID NO:2. Those polypeptides which are described are those polypeptides meeting the structural

requirements which also induce apoptosis or bind TRAIL or those consisting of the recited amino acid sequence. The portion of the genus which has not been described is that which meets the structural requirements of the claim but share no active function with SEQ ID NO:2 as well as the portion in which the region outside the specified amino acid sequence is the region conferring the recited function.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. There is not identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Which polypeptides of the genus comprising the required sequence are part of the invention has not been set forth.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be

unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only those polypeptides meeting the structural requirements which also induce apoptosis or bind TRAIL or those consisting of the recited amino acid sequence, but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claims 73, 74, 76-82, 84-91 and 93-98 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides comprising an amino acid sequence having at least 90% or 95% sequence identity with a particular disclosed sequence in which the functional limitation in the claims is directed to the amino acid sequence instead of the claimed polypeptide. The claims do not require that the polypeptide itself to possess any particular biological activity or conserved structure. The claims are drawn to a genus of polypeptides that is defined only by sequence identity and only a small subset of which have been described. Because the claims use the open language of a "polypeptide comprising", the claims are structurally very broad. There are a very large number of polypeptides which meet the structural requirements of the claim but share no active function with SEQ ID NO:2.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any

combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. In claims 73, 74, 76-82, 84-91 and 93-98, there is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Which polypeptides of the genus comprising the required sequence are part of the invention has not been set forth.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides consisting of the amino acid sequence sharing at least 90% identity with the recited fragment of SEQ ID NO:2 or comprising the particular recited fragments which are identical to the specified fragment of SEQ ID NO: 2 (*e.g.*, claim 75), but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath*

makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claim Objections

Claims 36, 45, 54, 75, 83, 92, 100 and 109 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 62-72, 117-126, 160-178 and 198-203 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 8:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.
Patent Examiner, Art Unit 1646
August 3, 2004

LORRAINE SPECTOR
PRIMARY EXAMINER